Public Health Goal for
OXAMYL
in Drinking Water

Prepared by

Pesticide and Environmental Toxicology Section
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

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LIST OF CONTRIBUTORS

PHG PROJECT MANAGEMENT	REPORT PREPARATION	SUPPORT
Project Officer Anna Fan, Ph.D. ***Chemical Prioritization Report Outline*** Joseph Brown, Ph.D. Coordinator David Morry, Ph.D. Yi Wang, Ph.D. ***Document Development*** Michael DiBartolomeis, Ph.D. Coordinator George Alexeeff, Ph.D. Hanafi Russell, M.S. Yi Wang, Ph.D. ***Public Workshop*** Michael DiBartolomeis, Ph.D. Coordinator Judy Polakoff, M.S. Organizer ***Methodology/Approaches/ Review Comments*** Joseph Brown, Ph.D. Robert Howd, Ph.D. Coordinators Lubow Jowa, Ph.D. David Morry, Ph.D. Rajpal Tomar, Ph.D. Yi Wang, Ph.D.	***Author*** Rajpal Tomar, Ph.D. ***Primary Reviewer*** Robert Howd, Ph.D. ***Secondary Reviewer*** Michael DiBartolomeis, Ph.D. ***Final Reviewers*** Anna Fan, Ph.D. William Vance, Ph.D. ***Editor*** Michael DiBartolomeis, Ph.D.	***Administrative Support*** Edna Hernandez Coordinator Laurie Bliss Sharon Davis Kathy Elliott Vickie Grayson Michelle Johnson Juliet Rafol Genevieve Shafer Tonya Turner ***Library Support*** Mary Ann Mahoney Valerie Walter ***Website Posting*** Robert Brodberg, Ph.D. Edna Hernandez Laurie Monserrat, M.S. Judy Polakoff, M.S. Hanafi Russell, M.S.

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PREFACE

Drinking Water Public Health Goal of the Office of Environmental Health Hazard Assessment

This Public Health Goal (PHG) technical support document provides information on health effects from contaminants in drinking water. The PHG describes concentrations of contaminants at which adverse health effects would not be expected to occur, even over a lifetime of exposure. PHGs are developed for chemical contaminants based on the best available toxicological data in the scientific literature. These documents and the analyses contained in them provide estimates of the levels of contaminants in drinking water that would pose no significant health risk to individuals consuming the water on a daily basis over a lifetime.

The California Safe Drinking Water Act of 1996 (amended Health and Safety Code, Section 116365) requires the Office of Environmental Health Hazard Assessment (OEHHA) to adopt PHGs for contaminants in drinking water based exclusively on public health considerations. The Act requires OEHHA to adopt PHGs that meet the following criteria:

1. PHGs for acutely toxic substances shall be set at levels at which scientific evidence indicates that no known or anticipated adverse effects on health will occur, plus an adequate margin-of-safety.
2. PHGs for carcinogens or other substances which can cause chronic disease shall be based solely on health effects without regard to cost impacts and shall be set at levels which OEHHA has determined do not pose any significant risk to health.
3. To the extent the information is available, OEHHA shall consider possible synergistic effects resulting from exposure to two or more contaminants.
4. OEHHA shall consider the existence of groups in the population that are more susceptible to adverse effects of the contaminants than a normal healthy adult.
5. OEHHA shall consider the contaminant exposure and body burden levels that alter physiological function or structure in a manner that may significantly increase the risk of illness.
6. In cases of scientific ambiguity, OEHHA shall use criteria most protective of public health and shall incorporate uncertainty factors of noncarcinogenic substances for which scientific research indicates a safe dose-response threshold.
7. In cases where scientific evidence demonstrates that a safe dose-response threshold for a contaminant exists, then the PHG should be set at that threshold.
8. The PHG may be set at zero if necessary to satisfy the requirements listed above.
9. OEHHA shall consider exposure to contaminants in media other than drinking water, including food and air and the resulting body burden.
10. PHGs adopted by OEHHA shall be reviewed periodically and revised as necessary based on the availability of new scientific data.

PHGs adopted by OEHHA are for use by the California Department of Health Services (DHS) in establishing primary drinking water standards (State Maximum Contaminant Levels, or MCLs). Whereas PHGs are to be based solely on scientific and public health considerations without regard to economic cost considerations, drinking water standards adopted by DHS are to consider economic factors and technical feasibility. For this reason PHGs are only one part of the information used by DHS for establishing drinking water standards. PHGs established by

OEHHA exert no regulatory burden and represent only non-mandatory goals. By federal law, MCLs established by DHS must be at least as stringent as the federal MCL if one exists.

PHG documents are developed for technical assistance to DHS, but may also benefit federal, state and local public health officials. While the PHGs are calculated for single chemicals only, they may, if the information is available, address hazards associated with the interactions of contaminants in mixtures. Further, PHGs are derived for drinking water only and are not to be utilized as target levels for the contamination of environmental waters where additional concerns of bioaccumulation in fish and shellfish may pertain. Often environmental water contaminant criteria are more stringent than drinking water PHGs, to account for human exposures to a single chemical in multiple environmental media and from bioconcentration by plants and animals in the food chain.

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SUMMARY

A Public Health Goal (PHG) of 50 ppb is developed for S-methyl N'N'-dimethyl-N-[(methyl-carbamoyl) oxy]-1-thiooxamimidate (oxamyl) in drinking water. The current state and federal Maximum Contaminant Levels (MCLs) for oxamyl are 200 ppb. The available toxicological data on oxamyl and the current drinking water regulations were reviewed in order to develop a PHG for oxamyl. A no-observed-adverse-effect level (NOAEL) of 2.5 mg/kg-day for decreased body weight gain in rats was selected as the critical dose. The PHG was calculated assuming a 10 kg child consuming one liter of water per day, a relative source contribution of 20% and an uncertainty factor of 100. Therefore, based on the scientific information available, a PHG for oxamyl of 0.05 mg/L (50 ppb) is calculated.

INTRODUCTION

Available scientific information on oxamyl was searched on Medline, Current Contents (from 1996 to July 1997), U.S. EPA's Integrated Risk Information System (IRIS), the Extoxnet (an on-line pesticide information system) and the Toxicology and Occupational Medicine System (TOMES, 1997). Articles thought to be of relevance to PHG determination were selected for review. The majority of the toxicological studies on oxamyl were conducted for the registration of oxamyl as a pesticide. Therefore, many of the studies meet the testing requirements of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) guidelines and are of good quality. These studies have been previously reviewed by U.S. EPA's Office of Pesticide and Water (U.S. EPA, 1992a,b), as well as by the California Department of Pesticide Regulation (DPR, 1992). Since these reviews were published, only two new relevant toxicity studies were identified from the scientific literature; these were also reviewed.

The current state MCL is 0.2 mg/L (200 ppb) which was adopted in 1993 (OEHHA, 1993) based on the U.S. Environmental Protection Agency's (U.S. EPA's) proposed MCL and Maximum Contaminant Level Goal (MCLG) (U.S. EPA, 1992a,b).

ENVIRONMENTAL OCCURRENCE

Oxamyl was not detected in 1,370 wells sampled in 34 counties in California. Sampling occurred between July 1, 1995 and June 30, 1996 (DPR, 1997). Oxamyl has been detected in ground water in Massachusetts, New York, New Jersey, and Rhode Island (U.S. EPA, 1992c).

TOXICOLOGY

Following acute oral exposure, oxamyl is extremely toxic to rats, mice and guinea pigs. In rats, the oral (gavage) LD_{50} of technical oxamyl ranged from 2.5 to 5.4 mg/kg. Oxamyl poisoning results in typical clinical signs of cholinesterase inhibition such as salivation, fasciculation and tremor prior to death. Fayez and Kilgore (1992) studied the effects of single acute oral doses of 1, 2.1 or 3.5 mg/kg on selected biochemical parameters in Sprague-Dawley rats. Body weight gains were significantly reduced during the first three days after gavage at 2.1 and 3.5 mg/kg, and at all dose levels at day 14. Brain and blood cholinesterase were significantly inhibited in the first few hours after dosing. Serum glucose-6-phosphatase and succinic acid dehydrogenase were inhibited at various time intervals. However, most of the biochemical parameters were not significantly

different at day 14. The cholinesterase inhibiting effect of oxamyl is short-term and reversible, as with other carbamates. This might explain the comparability of the acute oral LD_{50} of 2.5 mg/kg and the dietary exposure NOAEL of 2.5 mg/kg-day in rats.

In a chronic study, 36 weanling female and 36 weanling male rats were administered 0, 50, 100 or 150 ppm oxamyl in the diet for two years (Kennedy, 1986). An NOAEL of 50 ppm in the diet based on reduced body weight gain at 100 and 150 ppm was identified from this study. An NOAEL of 50 ppm was also observed in a combined chronic-oncogenicity study in rats (DPR, 1992) based on reduced body weight and increased hyperreactivity. In a two-year mouse study, an NOAEL of 25 ppm for reduced body weight was identified, and an NOAEL of 100 ppm for decreased serum alkaline phosphatase activity and cholesterol levels was identified from a chronic dog study (Kennedy 1986). An approximate NOAEL of 5 mg/kg was suggested by Kennedy (1986) for the chronic rat study presumably based on food consumption data. Because of the uncertainty associated with such data when measured intermittently by group during a chronic study, we used standard factors for converting ppm in diet to mg/kg-day for all chronic toxicity studies. For rats, mice and dogs, the factors for converting ppm in diet to mg/kg-day are 0.05, 0.15 and 0.025, respectively. Therefore, the converted NOAELs for the two rat, mouse and dog studies described above are 2.5, 2.5, 3.75 and 2.5 mg/kg, respectively.

Oxamyl was negative in various genotoxicity and mutagenicity tests and in long-term carcinogenicity studies in rats and mice. There is no scientific evidence that oxamyl is a teratogen. In a reproductive toxicity study, litter size and mean body weight of weanlings from dams fed 100 and 150 ppm levels of oxamyl were significantly decreased as compared to the control. No histopathological abnormalities were observed (Kennedy, 1986).

Iyaniwura (1991) studied cholinesterase inhibition by a combination of carbamate pesticides (carbofuran, oxamyl and propoxur) in rat plasma and erythrocytes *in vitro*. All three pesticide interactions were found to be additive. In another study, Iyaniwura (1989) studied the interaction of aldicarb, carbofuran and oxamyl on rat plasma cholinesterase inhibition *in vitro* by equal proportions of all three carbamates. The presence of carbofuran and aldicarb was found to reduce cholinesterase inhibition by oxamyl.

DOSE-RESPONSE ASSESSMENT

U.S. EPA's MCL was based on a NOAEL of 2.5 mg/kg-day oxamyl for decreased body weight gain at higher levels from a rat chronic toxicity study. An MCL of 0.2 mg/L was calculated based on a 70 kg adult male consuming two liter of water per day, a relative source contribution of 20% and an uncertainty factor of 100. From this calculation, the value of 0.175 mg/L was rounded by U.S. EPA to give a final MCL of 0.2 mg/L (200 ppb).

Following our review of the available scientific information, we concur with U.S. EPA's selection of the critical chronic rat study with an NOAEL of 2.5 mg/kg (Kennedy, 1986) for its MCL. This NOAEL is also supported by comparable NOAELs of 2.5, 3.75 and 2.5 mg/kg-day from a combined chronic/carcinogenicity study in rats and chronic mice and dog studies, respectively.

CALCULATION OF PHG

The following general equation for noncarcinogenic endpoints is used for calculating a public health-protective concentration (C) for oxamyl in drinking water:

$$C = \frac{NOAEL \times BW \times RSC}{UF \times L/day} = mg/L$$

where,

NOAEL	=	No-observed-adverse-effect-level (2.5 mg/kg-day)
BW	=	Body weight for a child (10 kg)
RSC	=	Relative source contribution of 20% (0.2) which is U.S. EPA's default value for organic chemicals
UF	=	Uncertainty factor of 100 (10-fold for inter-species variation and 10-fold for human variability)
L/day	=	Volume of daily drinking water consumption for a child (1 L/day).

Therefore,

$$C = \frac{2.5 \text{ mg/kg-day} \times 10 \text{ kg} \times 0.2}{100 \times 1 \text{ L/day}}$$

$$= 0.05 \text{ mg/L} = 50 \text{ ppb.}$$

Thus, OEHHA calculates and adopts a PHG of 0.05 mg/L (50 ppb) for oxamyl in drinking water.

RISK CHARACTERIZATION

Oxamyl is extremely acutely toxic. In most of the short-term and long-term toxicity studies, reduced body weight gain and hyperreactivity were the main long-term adverse effects. The available data support that oxamyl is not a mutagen, carcinogen or a teratogen. Litter size and mean body weight of weanlings from dams fed 100 and 150 ppm levels of oxamyl were significantly reduced compared to control levels in a reproductive toxicity study.

There are no human data on which to base the PHG for oxamyl. Therefore, it is based on animal studies. In extrapolating toxicity from animals to humans there is an inherent assumption that the data obtained in animals are relevant to humans. To account for inter- and intra-species variation, an uncertainty factor of 100 is used for calculating the PHG. The toxicity data for oxamyl is adequate and the observed NOAEL of 2.5 mg/kg-day in rats is consistent with data obtained from other rat, mice and dog studies, providing greater confidence in the NOAEL. No sensitive groups were identified for oxamyl. However, children may ingest a large amount of water within a short period of time and thus have potential for high acute exposure. Because of the closeness of acute LD_{50} values to the NOAEL, the PHG has been based on children's exposure. The margin of exposure for a child based on the dietary NOAEL of 2.5 mg/kg-day and the Public Health Goal of 0.05 mg/L is 500 (i.e., 2.5 mg/kg-day/0.05 mg/kg-day) and thus should provide enough margin of exposure to also protect against acute effects. Available data do not suggest synergistic effects of oxamyl with other organophosphate or carbamate pesticides. There are no reports available of contamination of drinking water with oxamyl.

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